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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
LOCKARD, JON MCCLELLAND	
ART UNIT	**PAPER NUMBER**
1647	

DATE MAILED: 12/28/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/056,405	ZWIEBEL, LAURENCE J.	
	Examiner	Art Unit	
	Jon M. Lockard	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 September 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *18-21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *18-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *12 September 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *10/17/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Application, Amendments, and/or Claims

1. The Amendment filed 12 September 2005 has been received and entered in full. Claims 16 and 19 are amended. Therefore, claims 16-19 remain pending and are the subject of this Office Action.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Information Disclosure Statement

3. The supplemental information disclosure statement filed on 17 October 2005 has been considered.

Withdrawn Objections and/or Rejections

4. The objection to the drawings as set forth at pg 2-3 of the previous Office Action (mailed 08 April 2005) is withdrawn in view of the amended drawings (filed 12 September 2005).

5. The rejection of claims 18 and 21 under 35 U.S.C. § 102(b) as being anticipated by Hyde et al. as set forth at pg 12 of the previous Office Action (mailed 08 April 2005) is withdrawn in view of Applicants amendment of said claims (filed 12 September 2005).

Maintained Objections and/or Rejections

Specification

6. The objection to the specification as set froth at pg 3 of the previous Office Action (mailed 08 April 2005) is maintained for reasons of record. It is noted that Applicant has amended the title within the first paragraph of the specification (filed 12 September 2005). However, Applicant must also formally amend the title of the Instant Application. For example, "The title of the application has been amended as follows: Mosquito Arrestin 1 Polypeptide ~~Olfactory Genes, Polypeptides, and Methods of Use Thereof~~" would be remedial.

Claim Rejections - 35 USC § 101

7. Claims 18-21 remain rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility, or a well established utility, for reasons set forth at pg 3-7 of the previous Office Action (mailed 08 April 2005).

8. The instant application discloses a nucleic acid set forth as SEQ ID NO:1 that encodes the protein set forth as SEQ ID NO:2. The specification asserts that SEQ ID NO:2 is an arrestin based on a conserved Src homology 3 binding site (See page 24, lines 1-3) and a high degree of homology to known Drosophila sequences (See page 33, lines 1-3). The instant specification does not teach any physiologic ligands or functional characteristics of the arrestin 1 set forth in SEQ ID NO:2 or encoded by the disclosed nucleic acid set forth in SEQ ID NO:1. There is no well-established utility for a specific nucleic acid or amino acid sequence and the specification fails to disclose a specific and substantial utility for the claimed invention.

9. Applicants argue at page 9 of the response (filed 12 September 2005) that the specification provides evidence that the claimed polypeptide has homology to known arrestins, and arrestins have a well-established use in biology based upon the protein's ability to ability to participate in the olfaction cascase. Thus, the Applicants argue, the claimed molecules are useful in assays to identify compounds which interfere with the olfaction cascade.

10. Applicant's arguments have been fully considered but they are not persuasive for the following reasons. It is noted that Applicant has not provided any evidence or reference of record to substantiate the allegation that the claimed protein set forth as SEQ ID NO:2 is involved in any olfaction cascade or that molecules that interact with it can be used to interfere in the olfaction cascade. It must be emphasized that arguments of counsel alone cannot take the place of evidence in the record once an examiner has advanced a reasonable basis for questioning the disclosure. See *In re Budnick*, 537 F.2d at 538, 190 USPQ at 424; *In re Schulze*, 346 F.2d 600, 145 USPQ 716 (CCPA 1965); *In re Cole*, 326 F.2d 769, 140 USPQ 230 (CCPA 1964). For example, in a case where the record consisted substantially of arguments and opinions of applicant's attorney, the court indicated that factual affidavits could have provided important evidence on the issue of enablement. See *In re Knowlton*, 500 F.2d at 572, 183 USPQ at 37; *In re Wiseman*, 596 F.2d 1019, 201 USPQ 658 (CCPA 1979).

11. Furthermore, while the Examiner agrees that it is credible that SEQ ID NO:2 is an arrestin, its identification as such is not sufficient to establish either a well-known, or a specific and substantial utility. As stated at pages 5-6 of the previous Office Action (mailed 08 April 2005), the art teaches that the beta arrestins show a high degree of homology between each other as well as to visual arrestins. The art also teaches that B-arrestin 1 and B-arrestin 2, for example,

have overlapping, but not identical, functions in both GPCR signaling and internalization. For example, in studies of second-messenger generation using mouse embryo fibroblasts (MEFs) obtained from embryos that lack B-arrestin 1, B-arrestin 2, or both proteins, cyclic AMP accumulation stimulated by B_2-adrenoceptor activation was enhanced in MEFs lacking one or the other B-arrestins, but was even more robustly enhanced in cells lacking both B-arrestins. Similarly, it was also shown that MEFs expressing the angiotensin AT_{1a} receptor, inositol phosphate accumulation elicited by angiotensin application was only modestly enhanced in the single knockouts, but was robustly enhanced in the double knockout MEFs. This suggests that, at least for desensitization of these two receptors, the B-arrestins might be interchangeable (Pierce et al. Classical and new roles of B-arrestins in the regulation of G-protein-coupled receptors. Nature Reviews. 2:727-733, 2001; See page 729, second paragraph). The art also teaches that although mammalian arrestin proteins cooperate with G protein-coupled receptor kinases (GRKs) in receptor desensitization, loss of *C. elegans* arrestin-1 does not disrupt chemosensation (Fukuto et al. G protein-coupled receptor kinase function is essential for chemosensation in *C. elegans*. Neuron 42:581-593, 2004). Similarly, Dolph (Arrestin: roles in the life and death of retinal neurons. The Neuroscientist 8(4):347-355, 2002) teaches that loss of Drosophila arrestin-1 had no effect on visual physiology or photoreceptor integrity.

12. Thus, although the homology of the arrestin family allows identification of such as arrestins, mere homology is not accepted by those of skill in the art as being predictive of function.. Utility must be in readily available form. It is possible that, after further characterization, this protein might be found to have a patentable utility, in which case proteins would have a specific utility, or the protein might be found to be associated with a specific

disease. This further characterization, however, is part of the act of the invention, and until it has been undertaken, Applicant's claimed invention is incomplete. Whereas one could readily employ the putative arrestin protein of the instant invention in an assay to identify ligands thereto, the information obtained from such assays would be of little use until one discovers the identity of those physiological processes moderated by that putative arrestin protein. Therefore, it is unclear as to what practical or real-world benefit is derived by the public from the identification of that ligand.

13. There is little doubt that, after further characterization, this protein may be found to have a specific and substantial credible utility. This further characterization, however, is part of the act of invention, and until it has been undertaken, Applicant's claimed invention is incomplete. The instant situation is directly analogous to that which was addressed in *Brenner v. Manson*, 148 U.S.P.Q. 689 (Sus. Ct, 1966), in which a novel compound which was structurally analogous to other compounds which were known to possess anti-cancer activity was alleged to be potentially useful as an anti-tumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation. However, the court held that this broad interpretation was not the intended definition of "useful" as it appears in 35 U.S.C. §101, which requires that an invention must have either an immediately obvious or fully disclosed "real world" utility. The court held that:

> "The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility", "[u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field", and "a patent is not a hunting license", "[i]t is not a reward for the search, but compensation for its successful conclusion."

14. Applicants argue at page 11 of the response (filed 12 September 2005) that since the Examiner acknowledged that the asserted utility is credible, then according to M.P.E.P. § 2107.01 III "if the asserted utility is credible, there is no basis to challenge such a claim on the basis that it lack utility under 35 U.S.C. 101".

15. Applicant's arguments have been fully considered but they are not persuasive for the following reasons. It is noted that M.P.E.P. § 2107.01 III also states that "pharmacological or therapeutic inventions that provide any "immediate benefit to the public" satisfy 35 U.S.C. § 101", in which case the molecules are understood to have a specific and substantial or well-known asserted utility. In the instant case, the specification of the Instant Application fails to disclose a specific and substantial utility for the claimed invention for reasons set forth above.

16. Applicant's arguments (filed 12 September 2005), as they pertain to the rejections have been fully considered but are not found to be persuasive for the following reasons. In the previous Office Action of 08 April 2005, the Examiner made a *prima facie* showing that the claimed invention lacks utility and provided sufficient evidentiary basis for factual assumptions relied upon in establishing the *prima facie* showing (see pages 3-7). The truth, or credibility, of the assertion of utility has not been questioned. Rather, the rejection sets forth that the assertion of utility is not specific or substantial. Essentially, Applicant has not provided evidence to demonstrate that the claimed polypeptide of the instant application is supported by a specific and asserted utility or a well-established utility. It is also noted that M.P.E.P. 2107.01 states:

> Deficiencies under the "useful invention" requirement of 35 U.S.C. 101 will arise in one of two forms. The first is where it is not apparent why the invention is "useful." This can occur when an applicant fails to identify any specific and substantial utility for the invention or fails to disclose enough information about the invention to make its usefulness immediately apparent to those familiar with the technological field of the invention. Brenner v. Manson, 383 U.S. 519, 148 USPQ 689 (1966); In re Ziegler, 992

> F.2d 1197, 26 USPQ2d 1600 (Fed. Cir. 1993). The second type of deficiency arises in the rare instance where an assertion of specific and substantial utility for the invention made by an applicant is not credible.

The Examiner has fully considered all evidence of record and has responded to each substantive element of Applicant's response.

Claim Rejections - 35 USC § 112, 1st Paragraph

17. Claims 18-21 also remain rejected under 35 U.S.C. 112, first paragraph for reasons set forth at page 7 of the previous Office Action (mailed 08 April 2005). Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

18. Furthermore, even if the polypeptide of SEQ ID NO:2 were to have a patentable utility, the instant disclosure would not be found to be enabling for the full scope of the claimed invention for reasons set forth at pages 7-9 in the previous Office Action (mailed 08 April 2005).

19. Claims 18, 20, and 21 are drawn to a genus of amino acid molecules comprising an amino acid sequence of conservatively modified SEQ ID NO:2 or an amino acid sequence of which comprises at least 40 consecutive residues of SEQ ID NO:2. However, other than the protein of SEQ ID NO:2, the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention

commensurate in scope with these claims as set forth at pages 7-9 in the previous Office Action (mailed 08 April 2005).

20. The Applicants traverse the rejection of claims 18, 20, and 21 at pg 10-11 of the response (filed 12 September 2005) on the grounds that the specification discloses how to make and use the currently claimed invention as currently amended.

21. The Applicant's arguments have been fully considered but are not found persuasive for the following reasons. The specification's disclosure is insufficient to enable one skilled in the art to practice the invention as broadly claimed without undue experimentation. The factors listed below have been considered in the analysis of enablement:

(A) The breadth of the claims;
(B) The nature of the invention;
(C) The state of the prior art;
(D) The level of one of ordinary skill;
(E) The level of predictability in the art;
(F) The amount of direction provided by the inventor;
(G) The existence of working examples; and
(H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

22. The claims are drawn to amino acid molecules comprising an amino acid sequence of conservatively modified SEQ ID NO:2 or an amino acid sequence of which comprises at least 40 consecutive residues of SEQ ID NO:2. While the disclosure provides general guidance on what constitutes a conservatively modified sequence, the disclosure has not shown (1) which portions of the protein of SEQ ID NO:2 are critical to the activity of the protein of SEQ ID NO:2 (which is itself unknown); (2) what modifications e.g., substitutions, deletions, or additions) one can make to SEQ ID NO:2 that will result in protein mutants or variants with the same function/activity as the claimed protein of SEQ ID NO:2; and (3) any guidance on how to use

mutants or variants of SEQ ID NO:2 which would, based on the language of said claims, encompass both active and inactive variants of SEQ ID NO:2, especially in the absence of any functional limitations in the claims.

23. As stated in the previous Office Action, The state of the art is such that the relationship between the sequence of a protein and its activity is not well understood and is unpredictable. Furthermore, it is known in the art that certain positions in the sequence are critical to the protein's structure/function relationship and can only tolerate only relatively conservative substitutions or no substitutions (See Wells, 1990, Biochemistry 29:8509-8517; Ngo et al., The Protein Folding Problem and Tertiary Structure Prediction, 1994, pp. 492-495). For example, analysis of deletion mutant of B-arrestin 2 demonstrated that the amino-terminus was required for optimal interaction of B-arrestin 2 with apoptosis signal-related kinase 1 (ASK1) and that the carboxyl-terminus was required for optimal interaction with c-Jun amino-terminus kinase 3 (JNK3) (McDonald et al. B-arrestin 2: a receptor-regulated MAPK scaffold for the activation of JNK3. Science 290:1574-1577, 2000). Similarly, site directed mutagenesis studies on visual arrestin have shown that there are specific regions which are critical to the binding of arrestin with the phosphorylated c-terminus of rhodopsin as well as the ability of arrestin to mobilize secondary binding sites (Gurevich et al. Visual arrestin binding to rhodopsin. The Journal of Biological Chemistry. 270(11):6010-6016, 1995).

24. Due to the large quantity of experimentation necessary to generate the infinite number of derivatives recited in the claims, the lack of direction/guidance presented in the specification regarding which structural features are required in order to provide activity, the absence of working examples directed to the same, the complex nature of the invention, the state of the prior

art which establishes the unpredictability of the effects of substitutions/deletions on protein structure and function, and the breadth of the claims which fail to recite any structural or functional limitations, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope, even if the protein of SEQ ID NO:2 were found to be enabled.

Claim Rejections - 35 USC § 112, 1st Paragraph (Written Description)

25. Claims 18, 20, and 21 also remain rejected under 35 USC 112, first paragraph for the reasons already of record on pages 9-11 of the previous Office Action (mailed 08 April 2005), as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

26. The specification discloses a protein of SEQ ID NO:2 and a nucleic acid sequence of SEQ ID NO:1 that encodes the protein of SEQ ID NO:2. However, claims 18 and 20 recite a protein comprising an amino acid sequence of conservatively modified SEQ ID NO:2, and claims 18 and 21 recite a protein comprising an amino acid sequence of which comprises at least 40 consecutive residues of SEQ ID NO:2. The claims do not require that the proteins possess any particular biological activity, nor any particular conserved structure, or other disclosed distinguishing feature. Thus, the claims are drawn to a genus of polypeptide molecules.

27. The Applicants traverse the rejection of claims 18, 20, and 21 at page 10-11 of the response (filed 12 September 2005) on the grounds that the specification discloses how to make and use the currently claimed invention as currently amended.

28. The Applicant's arguments have been fully considered but are not found persuasive for the following reasons. As stated at pages 9-11 of the previous Office Action, to provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, and any combination thereof. In this case, the only factor present in claims 18 and 20-21 is a partial structure in the form of a recitation of conservatively modified or "comprises at least 40 consecutive residues of SEQ ID NO:2". The specification does not identify any particular structure/function correlation or biological activity. The distinguishing characteristics of the claimed genus are not described. The only adequately described species is the polypeptide set forth as SEQ ID NO:2. Accordingly, the specification does not provide adequate written description of the claimed genus.

29. *Vas-Cath Inc. v. Mahurkar*, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116).

30. With the exception of the sequences referred to above, the skilled artisan cannot envision the detailed chemical structure of the encompassed polypeptides molecules, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The nucleic acid itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

31. One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

32. Therefore, only the polypeptide set forth as SEQ ID NO:2, but not the full breadth of the claims meet the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Summary

33. No claim is allowed.

34. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Jon M. Lockard, Ph.D.** whose telephone number is **(571) 272-2717**. The examiner can normally be reached on Monday through Friday, 8:00 AM to 6:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Brenda Brumback**, can be reached on **(571) 272-0961**.

The fax number for the organization where this application or proceeding is assigned is **571-273-8300**.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see **http://pair-direct.uspto.gov**. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at **866-217-9197** (toll-free).

JML
December 21, 2005

LORRAINE SPECTOR
PRIMARY EXAMINER